



Medical Coverage Policy

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Coverage Policy Number 0028

Plasma Brain Natriuretic Peptide in the Outpatient Setting

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Related Coverage Resources

[Atherosclerotic Cardiovascular Disease Risk Assessment: Emerging Laboratory Evaluations](#)

INSTRUCTIONS FOR USE

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Overview

This Coverage Policy addresses measurement of plasma brain natriuretic peptide (BNP) or NT-proBNP in an outpatient setting as an adjunct to other clinical testing.

Coverage Policy

The measurement of plasma brain natriuretic peptide (BNP) or NT-proBNP in an outpatient setting as an adjunct to other clinical testing is considered medically necessary for ANY of the following indications:

- to distinguish between heart failure (HF) and primary lung disease in a dyspneic individual
- establishing prognosis or disease severity in chronic HF
- monitoring response to treatment for HF to achieve optimal dosing of guideline directed medical therapy (GDMT)
- risk stratification in a suspected acute coronary syndrome (ACS)

Plasma brain natriuretic peptide (BNP) or NT-proBNP testing in an outpatient setting for any other indication is considered experimental, investigational or unproven.

General Background

Brain-type natriuretic peptide (BNP) or N-terminal (NT) pro hormone BNP (NT-proBNP) testing has been proposed as an adjunct to other clinical testing in numerous clinical situations including, but not limited to, to aid in the diagnosis of patients presenting to the emergency department with acute dyspnea, monitor response to treatment for heart failure, and as a prognostic indicator in the risk stratification of individuals with suspected acute coronary syndromes (ACS). In addition, it has been proposed as a tool to screen asymptomatic adults in the general population for heart failure.

BNP is produced mainly in the cardiac ventricle. Secretion of both BNP and NT-proBNP is enhanced by ventricular wall stretch and volume overload, as occur in heart failure. Plasma levels of BNP are less than 100pg/mL in most healthy individuals; reference ranges depend on age and gender. NT proBNP: 0-74 years of age: ≤ 124 pg/mL; 75 years of age and older: ≤ 449 pg/mL. Assays for both BNP and NT-proBNP are available; a clear advantage of one biomarker over the other for any particular application has not been established. The established application of BNP measurement is for diagnosing acutely ill patients presenting to emergency service with shortness of breath. A major limitation of BNP is that a wide range of values is observed in patients with and without HF, and all of the determinants of the circulating BNP level have not yet been well established. BNP is increased in conditions of fluid imbalance other than heart failure, particularly renal insufficiency, which commonly coexists with heart failure. In individuals without heart failure, higher levels are associated with female gender, advanced age, and lower body mass index.

U.S. Food and Drug Administration (FDA)

A number of devices have received FDA 510(k) approval for evaluating circulating BNP and NT-proBNP levels. These devices can be found on the FDA Center for Devices and Radiological Health 510(k) database. An example of an FDA-approved BNP device is the Triage[®] B-Type Natriuretic Peptide (BNP) Test (Biosite, Inc., San Diego, CA). The test is intended to be used as an aid in the following (FDA, 2005):

- diagnosis of heart failure
- assessment of heart failure severity
- risk stratification of patients with acute coronary syndromes (ACS)
- risk stratification of patients with heart failure

The clinical supportive data in the 510(k) substantial equivalence determination decision summary device only template states the sponsor provided five peer-reviewed articles assessing the clinical utility of BNP measurements as an aid in the risk stratification of patients with heart failure. The references are not listed for the five articles but can be found in the sponsor labeling. The decision summary states that a systematic review by Doust et al. (2005) included the five articles previously mentioned which concluded that BNP was a strong prognostic indicator for patients with heart failure (FDA, 2005).

An example of a NT-proBNP test system is the Elecsys[®] proBNP Immunoassay (Roche Diagnostics Corporation, Indianapolis, IN). The intended use is as an aid in the diagnosis of individuals suspected of having CHF. The test is further indicated for the risk stratification of patients with ACS and CHF. Three peer-reviewed studies are listed as clinical supportive data in the 510(k) substantial equivalence determination decision summary device only template including James et al. (2003), Jernberg et al. (2002), and Fisher et al. (2003) (FDA, 2003).

Heart Failure

Heart failure is traditionally diagnosed by a history and physical examination. Supplementary diagnostic testing includes chest radiography, echocardiography, right-sided heart catheterization, and the six-minute walk test. A simple, rapid and objective test that can be conducted at the point of care to aid diagnosis is valuable to the clinician, as there may be many reasons for a patient's sudden onset of shortness of breath. Therefore, natriuretic peptides have been researched for such a test due to their ability to aid in the diagnosis and management of heart failure. A prognosis in heart failure is generally made by calculating a patient's heart failure

survival score (HFSS), which combines the results of commonly obtained, noninvasive, objective tests to stratify the patient's risk of future morbidity and mortality (Cardarelli and Lumicao, 2003; Aaronson, et al., 1997).

Literature Review Heart Failure

Studies have evaluated the diagnostic, prognostic and therapeutic monitoring value of BNP and NT-proBNP testing in patients with heart failure. Plasma BNP and NT-proBNP concentrations correlate with elevated end-diastolic pressure, which closely parallels dyspnea in heart failure. This suggests that these biomarkers are uniquely suited to provide accurate neurohormonal profiling in heart failure, increasing as heart failure progresses. Normal BNP or NT-proBNP levels have a high negative predictive value for the exclusion of heart failure. Use of these tests to rule out heart failure may save the patient from additional invasive and uncomfortable testing for heart failure, such as echocardiogram and right heart catheterization, and allow care to focus on other reasons for shortness of breath. In patients with elevated BNP or NT-ProBNP levels, the degree of elevation correlates with the severity of heart failure, according to the New York Heart Association* classification system. BNP is elevated in patients who have right heart failure, but the degree of elevation is not as great as BNP elevation from left ventricular dysfunction. BNP levels may also be affected by age, sex, weight, and renal function (ICSI, 2013; Hunt, et al., 2009; Christ, et al., 2006; Krauser, 2005; Winter and Elin, 2004).

***New York Heart Association Functional Classification of Patients with Heart Disease**

Classification	Characteristics
Class I	No limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation or dyspnea.
Class II	Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in fatigue, palpitation, or dyspnea.
Class III	Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity causes fatigue, palpitation, and dyspnea.
Class IV	Inability to carry on any physical activity without discomfort. Symptoms of cardiac insufficiency at rest. If any physical activity is undertaken, discomfort is increased.

Masson et al. (2006) performed a direct comparison of BNP and NT-proBNP in patients with chronic and stable heart failure. The authors reported that both natriuretic peptides showed subtle differences in their relation to clinical characteristics and prognostic performance. NT-proBNP performed slightly better than BNP for predicting outcome, in particular for death from pump failure and hospitalization for heart failure.

Diagnosis of Heart Failure: The use of BNP or NT-proBNP as an adjunct in diagnosing heart failure in patients presenting to an acute care setting with dyspnea has been studied in several large trials. At a cutoff from 80–100 picograms/milliliter (pg/mL), BNP has a sensitivity of approximately 90%, specificity of approximately 73%, and diagnostic accuracy of approximately 81–83% (Januzzi, et al., 2019; Roberts, et al., 2015; Moe, et al., 2007; Januzzi, et al., 2006; Baggish, et al., 2006; Mueller, et al., 2005; Lainchbury et al., 2003; Wright, et al., 2003; Maisel, et al., 2002; Morrison, et al., 2002; McCullough, et al., 2002; Dao, et al., 2001).

Prognosis in Heart Failure: Many patients who have been hospitalized with acute exacerbations of heart failure have multiple rehospitalizations. The use of BNP and NT-proBNP testing may be a prognostic marker for morbidity and mortality in these patients. There is evidence in the published, peer-reviewed scientific literature that supports the clinical utility of BNP and NT-proBNP testing at the time of symptom presentation as a prognostic indicator for patients with heart failure (Januzzi, et al., 2006; Harrison, et al., 2002; Koglin, et al., 2001).

Doust et al. (2005) conducted a systematic review of the literature detailing the potential for BNP to be used as a predictor of cardiac events and death in patients with heart failure. A total of 19 studies that used BNP values to estimate the relative risk of death or other cardiovascular events in heart failure patients and five studies that predicted risk in asymptomatic patients were included in the analysis. In heart failure patients, each increment of 100 pg/ml in BNP values was associated with a 35% increase in the relative risk of death. In 35 multivariate

analysis models, BNP or NT-proBNP was the only variable to reach significance as a predictor in nine of them, meaning that other variables did not contain further prognostic information beyond the information provided by BNP/NT-proBNP. The authors reported that, although systematic reviews of prognostic studies have difficulties such as publication bias (i.e., lack of publication of negative results), BNP is a strong predictor of adverse outcomes in both asymptomatic and heart failure patients.

Monitoring Treatment for Heart Failure: While published data supporting the clinical utility of BNP and NT-proBNP testing in the management of patients with heart failure are limited, measurement of BNP levels as an adjunct to standard testing for monitoring the effectiveness of therapy for patients with heart failure has become the accepted standard in many heart failure clinics (Porapakham, et al., 2010; Jourdain, et al., 2007; Troughton, et al., 2000; Murdoch, et al., 1999).

Screening for Heart Failure: The use of BNP testing as a tool to screen asymptomatic individuals in the general population for heart failure is still under study. Impact on meaningful health outcomes is not yet known. Additional well-designed clinical trials are needed before the role of this of this testing in the general asymptomatic population can be established.

Hill et al. (2008) conducted a systematic review of randomized controlled trials and observational studies to determine the screening and diagnostic properties of BNP and NT-proBNP for heart failure in primary care. The researchers calculated sensitivity, specificity, positive and negative likelihood ratios, area under the receiver–operator characteristic curve and diagnostic odds ratio. The review included 17 studies (i.e., seven screening, nine diagnosis in primary care or specialized clinic, one both). There was heterogeneity within the study populations, reference standard for diagnosis, and B-type natriuretic peptide decision point. These studies involved patients from various and diverse populations. The reference standard for the diagnosis of heart failure is not consistent among studies. Similarly, the decision points for BNP and NT-proBNP in the diagnosis of heart failure are also not consistent. This, and the small number of studies, made meta-analysis within the two groups impractical. Sensitivity ranged from 26% to 98%; and specificity from 44% to 88%. For screening, the diagnostic odds ratio ranged from 2.7—29, and for diagnosis from 2.8—137. The authors reported that the performance characteristics of B-type natriuretic peptides measurement are not suitable for screening asymptomatic patients. For diagnosis in primary care, low B-type natriuretic peptide values may be used to rule-out heart failure but, due to poor specificity, high values cannot be used to rule-in the condition.

Acute Coronary Syndromes (ACS)

Patients with ACS include those whose clinical presentations cover the following range of diagnoses: unstable angina, non–ST-elevation myocardial infarction, and ST-elevation myocardial infarction. The medical history, physical examination, electrocardiogram, assessment of renal function, and cardiac biomarker measurements in patients with symptoms suggestive of ACS at the time of the initial presentation can be integrated into an estimation of the risk of death and nonfatal cardiac ischemic events (Anderson, et al., 2013). Natriuretic peptides, which have been mainly used in the diagnosis of heart failure, have also been found to be elevated in patients with ACS. It has been reported that elevated BNP and NT-proBNP levels at admission in patients with ACS are associated with poor prognosis, including increased mortality, development of heart failure, and recurrent ischemic events (Kwan, et al., 2007).

Literature Review: There is sufficient evidence in the published, peer-reviewed scientific literature to support the clinical utility of BNP and NT-proBNP testing at the time of symptom presentation as a prognostic indicator for patients with an ACS. Additional studies are needed to identify therapies that may modify the risk associated with increased levels of BNP and NT-proBNP testing in ACS (Omland, 2007; Body, et al., 2006; Richards, et al., 2003; Jernberg, et al., 2003; James, et al., 2003; Morrow, et al., 2003; De Lemos, et al., 2001).

Other Indications

There is some evidence to suggest that BNP levels may be useful in evaluating surgical indications in pediatric patients with ventricular septal defect (Kunii, et al., 2003). BNP levels may provide valuable information for the detection of infants with significant patent ductus arteriosus who require treatment (Kulkarni, et al., 2015; Choi, et al., 2005). BNP may provide future usefulness as a screening tool for left-ventricular dysfunction (McDonagh, et al., 1998, 2001; Maisel, et al., 2001; Vasan, et al., 2002; Hedberg, et al., 2004; DeLemos, et al., 2009) or as a prognostic tool before the onset of clinically apparent cardiovascular disease (Wang, et al., 2004). BNP has been

studied as a tool to assess outcomes in patients without heart failure who undergo atrial fibrillation ablation (Kuroski, et al., 2007). The usefulness of NT-proBNP levels is being studied as stroke risk prediction in anticoagulated patients with atrial fibrillation (Roldán, et al., 2014). Proposed uses of NT-proBNP include cardiac disease and dysfunction detection in the asymptomatic patient (Galvani, et al., 2004; Hartmann, et al., 2004; Pfister, et al., 2004; Bay, et al., 2003; Kragelund, et al., 2005; Singh, et al., 2009) and risk stratification in hypertension (Hildebrandt, et al., 2004; Olsen, et al., 2004). BNP is being investigated as a biomarker for the diagnosis and risk stratification of patients with septic shock (Kandil, et al., 2008). BNP has been proposed to predict the prognosis of persons with coronary artery disease (Oremus, et al., 2008) and as a preoperative and postoperative risk stratification tool for a subgroup of patients at high risk of death and major adverse cardiovascular event from major noncardiac surgery (Khurshaidi, et al., 2020; Rodseth, et al., 2013; Ryding, et al., 2009). High NT-proBNP level is being investigated as a major risk factor for death in patients with sickle cell disease (Machado, et al., 2011). As a biomarker of clinical, laboratory, and echocardiographic abnormalities in children with homozygous sickle cell disease (Takatsuki, et al., 2012). The prognostic value of NT-proBNP in unselected critically ill patients with acute respiratory failure (ARF) is being investigated (Okkonen, et al., 2011). BNP along with other cardiac biomarkers has been proposed to predict right ventricular dysfunction in patients with acute pulmonary embolism (Baja, et al., 2015; Gutte, et al., 2010). NT-proBNP is being investigated as a predictor of long-term survival in male patients of 75 years and older with high-grade asymptomatic internal carotid artery stenosis (Duschek, et al., 2011). The association between BNP levels in blood and risk of type 2 diabetes is being investigated (Pfister, et al., 2011). The utility of BNP levels are being investigated in preeclampsia (Afshani, et al., 2013), in all-cause mortality after stroke (García-Berrococo, et al., 2013) and occurrence of atrial fibrillation after cryptogenic stroke (Rodríguez-Yáñez, et al., 2013). NT-proBNP is being investigated as a biomarker to assess cardiac function in adults with corrected tetralogy of Fallot (Eindhoven, et al., 2014). As a diagnostic tool in acute Kawasaki disease (Lin, et al., 2015). As a biomarker of cardiovascular stress in patients with aortic stenosis undergoing valve replacement (Lindam, et al., 2015). N-terminal pro-B-type natriuretic peptide as a prognostic tool for patients with adult congenital heart disease (Baggen, et al., 2017). Screening for late pulmonary hypertension in infants with bronchopulmonary dysplasia (Behere, et al., 2019). Diagnosing pulmonary hypertension in severe bronchopulmonary dysplasia (Avitabile, et al., 2019). BNP or NT-proBNP is being investigated as a predictive marker for contrast-induced acute kidney injury (CI-AKI) in patients with acute coronary syndrome (ACS) undergoing coronary angiography (Li, et al., 2020). In a meta-analysis, Pranata et al. (2020) suggests elevated NT-proBNP level is associated with increased mortality in COVID-19 pneumonia. Currently, there are limited data to support these indications. Additional research is needed to define the role of BNP and NT-proBNP in these clinical situations.

Professional Societies/Organizations

In 2017, the American College of Cardiology (ACC) and the American Heart Association (AHA) published a focused update to the 2013 diagnosis and management of heart failure in adults practice guideline (Yancy, et al., 2017).

The subsection of the guideline which addresses initial and serial evaluation of the heart failure (HF) patient categorizes the role of biomarkers into prevention, diagnosis, prognosis, and added risk stratification to clarify evidence-based objectives of their use in clinical practice. Natriuretic peptide biomarker recommendations include the following:

Diagnosis

Class I, Level of Evidence A

- In patients presenting with dyspnea, measurement of natriuretic peptide biomarkers is useful to support a diagnosis or exclusion of HF. This is a modified recommendation. The 2013 acute and chronic recommendations have been combined into a diagnosis section.

Prognosis or Added Risk Stratification

Class I, Level of Evidence A

- Measurement of BNP or NT-proBNP is useful for establishing prognosis or disease severity in chronic HF. The 2013 recommendation remains current.

- Measurement of baseline levels of natriuretic peptide biomarkers and/or cardiac troponin on admission to the hospital is useful to establish a prognosis in acutely decompensated HF. The current recommendation emphasizes that it is admission levels of natriuretic peptide biomarkers that are useful. This is a modification from the 2013 guideline recommendation.

Class IIa, Level of Evidence B-NR

- During a HF hospitalization, a predischarge natriuretic peptide level can be useful to establish a postdischarge prognosis. This current recommendation is new.

Prevention of Heart Failure

Class IIa, Level of Evidence B-R

- For patients at risk of developing HF, natriuretic peptide biomarker–based screening followed by team-based care, including a cardiovascular specialist optimizing guideline directed medical therapy (GDMT), can be useful to prevent the development of left ventricular dysfunction (systolic or diastolic) or new-onset HF. This is a new recommendation.

Class (Strength) of Recommendation:

Class I (Strong) Benefit >>>>Risk

Class IIa (Moderate) Benefit>>Risk

Class IIb (Weak) Benefit > Risk

Class III No Benefit (Moderate) Benefit=Risk

Class III Harm (Strong) Benefit>Risk

Level (Quality) of Evidence:

Level A if the data were derived from high-quality evidence from more than one randomized clinical trial, meta-analyses of high-quality randomized clinical trials, or one or more randomized clinical trials corroborated by high-quality registry.

Level B-R when data were derived from moderate quality evidence from one or more randomized clinical trials, or meta-analyses of moderate-quality randomized clinical trials.

Level B-NR is used to denote moderate-quality evidence from one or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies. This designation was also used to denote moderate-quality evidence from meta-analyses of such studies.

Level C-LD when the primary source of the recommendation was randomized or nonrandomized observational or registry studies with limitations of design or execution, meta-analyses of such studies, or physiological or mechanistic studies of human subjects.

Level C-EO was defined as expert opinion based on the clinical experience of the writing group.

The 2020 ACC/AHA Guideline for the Management of Patients With Valvular Heart Disease states that an elevated serum BNP level is a marker of subclinical HF and LV decompensation. In a cohort of 387 asymptomatic adults with severe aortic stenosis (AS), elevated BNP levels were associated with an increased 5-year risk of AS-related events, with a hazard ratio for a BNP level >300 pg/mL (3 times normal) of 7.38. Serum BNP levels also are predictive of symptom onset during follow-up and persistent symptoms after aortic valve replacement (ACC, 2020).

The American Heart Association 2017 Scientific Statement ‘Role of Biomarkers for the Prevention, Assessment, and Management of Heart Failure’ (Chow, et al., 2017) notes that monitoring natriuretic peptide concentrations in blood not only can provide the clinician information about the diagnosis and severity of HF but also can improve prognostication and treatment strategies.

The 2014 AHA/ACC Guideline for the Management of Patients With Non–ST-Elevation Acute Coronary Syndromes (ACS) recommends that BNP or NT–pro-BNP may be considered to assess risk in patients with suspected ACS (Class IIa, Level of evidence B). A class IIa, level of evidence B recommendation indicates it is reasonable to perform the procedure/administer the treatment. The benefit outweighs the risk, but additional studies with focused objectives are needed. The recommendation is in favor of the treatment or procedure being useful/effective, with some conflicting evidence from single randomized trial or nonrandomized studies.

In the section of the guideline that addresses cardiac biomarkers and the universal definition of MI BNP recommendations state that BNP may be reasonable for additional prognostic information (Class IIb, Level of evidence B). A class IIb, level of evidence B recommendation indicates the procedure/treatment may be considered. The benefit is equal to or greater than the risk. Additional studies with broad objectives needed; additional registry data would be helpful. The usefulness/efficacy is less well established, with greater conflicting evidence from single randomized trial or nonrandomized studies (Amsterdam, et al., 2014).

In 2012, the ACC/AHA published a focused update to their 2007 guidelines for the management of patients with unstable angina/non-ST elevation myocardial infarction. In the recommendations for early risk stratification, the authors added B-type natriuretic peptides as a newer biomarker. The recommendation states that measurement of BNP or NT-proBNP may be considered to supplement assessment of global risk in patients with suspected acute coronary syndrome (ACS). The guidelines state that numerous prospective studies and data from large data sets have documented B-type natriuretic peptides' powerful prognostic value independent of conventional risk factors for mortality in patients with stable and unstable coronary artery disease. The guideline states that "studies in ACS showed that when measured at first patient contact or during the hospital stay, the natriuretic peptides are strong predictors of both short- and long-term mortality in patients with ST elevation myocardial infarction or unstable angina/non-ST elevation myocardial infarction" (Anderson, et al., 2013). There has been no update to this guideline since 2012.

American Association for Clinical Chemistry (AACC): The AACC (formerly the National Academy of Clinical Biochemistry) Practice Guidelines address B-Type Natriuretic Peptide:

- Emerging Biomarkers for Primary Prevention of Cardiovascular Disease and Stroke (2009) recommendations state that more research should be performed to determine if BNP and NT-proBNP are useful in identifying individuals who are at increased risk of developing heart failure and might benefit from therapies for prevention. The guidelines were developed by a multidisciplinary expert panel after systematically reviewing available evidence and evaluating criteria of clinical usefulness, consistency of epidemiologic data, improved predictive value, independence from other factors, and available analytical methods. When possible, the recommendations were based on prospective observational studies of healthy populations. Retrospective studies or studies consisting of populations with vascular disease were only considered for secondary prevention. The strength of data was characterized using the criteria from the American Heart Association (AHA)/American College of Cardiology (ACC). There has been no update to this guideline since 2009.
- Use of Cardiac Troponin and B-Type Natriuretic Peptide or N-Terminal proB-Type Natriuretic Peptide for Etiologies Other than Acute Coronary Syndromes and Heart Failure (Wu, et al., 2007) recommendations state that routine BNP/NT-proBNP measurement is not warranted in asymptomatic end stage renal disease patients, patients undergoing noncardiac surgery or among patients undergoing percutaneous coronary intervention. At this time, there is insufficient evidence to recommend routine measurement of BNP/NT-proBNP before or after cardiac surgery. Routine BNP/NT-proBNP measurements may be warranted among patients with nonischemic etiologies such as sepsis, myocarditis, or pulmonary embolism but the weight of evidence is based on expert consensus as the primary basis for the recommendation. There has been no update to this guideline since 2007.

The American Board of Internal Medicine's (ABIM) Foundation Choosing Wisely® Initiative

No information found.

Use Outside of the US

The Heart Failure Association of the European Society of Cardiology Practical Guidance on the use of natriuretic peptide concentrations (Mueller, et al., 2019) lists 'Key principles' for the use of natriuretic peptides (NPs) in clinical practice:

- NPs should always be used in conjunction with all other clinical information
- NPs are reasonable surrogates for intracardiac volumes and filling pressures
- NPs should be measured in all patients presenting with symptoms suggestive of HF such as dyspnoea and/or fatigue, as their use facilitates the early diagnosis and risk stratification of HF

- NPs have very high diagnostic accuracy in discriminating HF from other causes of dyspnoea: the higher the NP, the higher the likelihood that dyspnoea is caused by HF
- Optimal NP cut-off concentrations for the diagnosis of acute HF (very high filling pressures) in patients presenting with acute dyspnoea to the emergency department are higher as compared with those used in the diagnosis of chronic HF in patients with dyspnoea on exertion (mild increase in filling pressures at rest)
- Obese patients have lower NP concentrations, mandating the use of lower cut-off concentrations (about 50% lower)
- In stable HF patients, but also in patients with other cardiac disorders such as myocardial infarction, valvular heart disease, atrial fibrillation, or pulmonary embolism, NP concentrations have high prognostic accuracy for death and HF hospitalization
- Screening with NPs for the early detection of relevant cardiac disease including left ventricular systolic dysfunction in patients with cardiovascular risk factors may help identify patients at increased risk, therefore allowing targeted preventive measures to prevent HF
- BNP, NT-proBNP and MR-proANP have comparable diagnostic and prognostic accuracy
- In patients with shock, NPs cannot be used to identify cause (e.g. cardiogenic vs. septic shock), but remain prognostic
- NPs cannot identify the underlying cause of HF and therefore, if elevated, must always be used in conjunction with cardiac imaging

The ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure addresses diagnostic tests in patients with heart failure (HF). The recommendations state that natriuretic peptides are recommended/should be considered for initial assessment of a patient with newly diagnosed HF in order to evaluate the patient's suitability for particular therapies, to detect reversible/treatable causes of HF and comorbidities interfering with HF.

- A Class IIa, Level of Evidence C recommendation indicates that the weight of evidence/opinion is in favor of usefulness/efficacy. Consensus of opinion of the experts and/or small studies, retrospective studies, registries (Ponikowski, et al., 2016).

Canadian Cardiovascular Society (CCS): The 2017 Comprehensive Update of the Canadian Cardiovascular Society Guidelines for the Management of Heart Failure addresses biomarkers/natriuretic peptides (NP) including the following recommendations (Ezekowitz, et al., 2017).

Diagnosis and management of heart failure (HF):

- BNP/NT-proBNP levels be measured to help confirm or rule out a diagnosis of HF in the acute or ambulatory care setting in patients in whom the cause of dyspnea is in doubt (Strong Recommendation; High-Quality Evidence).
- Measurement of BNP/NTproBNP levels be considered in patients with an established diagnosis of heart failure with reduced EF (HFrEF) for prognostic stratification, in view of optimizing medical therapy (Strong Recommendation; High-Quality Evidence).

Management of chronic HFrEF:

- Suggest that in ambulatory patients with HFrEF measurement of BNP or NT-proBNP to guide management should be considered to decrease HF related hospitalizations and potentially reduce mortality. The benefit is uncertain in individuals older than 75 years of age (Weak Recommendation; Moderate-Quality Evidence).

Management of decompensated chronic HFrEF:

- Suggest that measurement of BNP or NTproBNP in patients hospitalized for HF should be considered before discharge, because of the prognostic value of these biomarkers in predicting rehospitalization and mortality (Strong Recommendation; Moderate-Quality Evidence).

National Institute for Health and Clinical Excellence (NICE) (United Kingdom): NICE Clinical Guidance on Chronic Heart Failure in Adults; Diagnosis and Management updated in 2018 addresses the diagnosis of heart failure. The recommendations for serum natriuretic peptides state: "Take a careful and detailed history, and

perform a clinical examination and tests to confirm the presence of heart failure. Measure serum natriuretic peptides (B-type natriuretic peptide [BNP] or N-terminal pro-B-type natriuretic peptide [NTproBNP]) in patients with suspected heart failure. Because very high levels of serum natriuretic peptides carry a poor prognosis, refer patients with suspected heart failure and a BNP level above 400 pg/ml (116 pmol/litre) or an NTproBNP level above 2000 pg/ml (236 pmol/litre) urgently, to have transthoracic Doppler 2D echocardiography and specialist assessment within 2 weeks. Refer people with suspected heart failure and an NT-proBNP level between 400 and 2,000 ng/litre (47 to 236 pmol/litre) to have specialist assessment and transthoracic echocardiography within 6 weeks.” (NICE, 2018).

NICE Clinical Guidance on Acute Heart Failure in Adults (2014) states in people presenting with new suspected acute heart failure, use a single measurement of serum natriuretic peptides (B-type natriuretic peptide [BNP] or N-terminal pro-B-type natriuretic peptide [NT-proBNP]) and the following thresholds to rule out the diagnosis of heart failure:

- BNP less than 100 ng/litre
- NT-proBNP less than 300 ng/litre.

NICE checked this guideline in December 2017 and found no new evidence that affects the recommendations in this guideline.

Medicare Coverage Determinations

	Contractor	Determination Name/Number	Revision Effective Date
NCD		No National Coverage Determination found	
LCD	CGS Administrators, LLC	B-type NATRIURETIC PEPTIDE (BNP) Testing (L33943)	11/28/2019
LCD	National Government Services, Inc	B-type NATRIURETIC PEPTIDE (BNP) Testing (L33573)	11/07/2019
LCD	First Coast Services Options, Inc.	B-Type NATRIURETIC PEPTIDE (BNP) (L33267)	01/08/2019
LCD	Noridian Healthcare Services	B-type NATRIURETIC PEPTIDE (BNP) Testing (L35526)	10/01/2019
LCD	Palmetto GBA	B-type NATRIURETIC PEPTIDE (BNP) Testing (L34410)	01/14/2021
LCD	Noridian Healthcare Solutions, Inc.	B-type NATRIURETIC PEPTIDE (BNP) Testing (L34038)	10/01/2019
LCD	Palmetto GBA	Brain NATRIURETIC PEPTIDE (BNP) Level (L33422)	10/10/2019

Note: Please review the current Medicare Policy for the most up-to-date information.

Coding/Billing Information

Note: 1) This list of codes may not be all-inclusive.

2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

CPT®* Codes	Description
83880	Natriuretic peptide

ICD-10-CM Diagnosis Codes	Description
I11.0-I11.9	Hypertensive heart disease
I20.0	Unstable angina
I21.01- I21.09	ST elevation (STEMI) myocardial infarction of anterior wall
I21.11- I21.19	ST elevation (STEMI) myocardial infarction of inferior wall
I21.21- I21.4	ST elevation (STEMI) myocardial infarction of other sites
I22.0-I22.9	Subsequent ST elevation (STEMI) and non-ST elevation (NSTEMI) myocardial infarction
I24.0	Acute coronary thrombosis not resulting in myocardial infarction
I24.8	Other forms of acute ischemic heart disease
I24.9	Acute ischemic heart disease, unspecified
I25.110	Atherosclerotic heart disease of native coronary artery with unstable angina pectoris
I25.700	Atherosclerosis of coronary artery bypass graft(s), unspecified, with unstable angina pectoris
I25.710	Atherosclerosis of autologous vein coronary artery bypass graft(s) with unstable angina pectoris
I25.720	Atherosclerosis of autologous artery coronary artery bypass graft(s) with unstable angina pectoris
I25.730	Atherosclerosis of nonautologous biological coronary artery bypass graft(s) with unstable angina pectoris
I25.750	Atherosclerosis of native coronary artery of transplanted heart with unstable angina
I25.760	Atherosclerosis of bypass graft of coronary artery of transplanted heart with unstable angina
I25.790	Atherosclerosis of other coronary artery bypass graft(s) with unstable angina pectoris
I27.0	Primary pulmonary hypertension
I42.0-I42.9	Cardiomyopathy
I50.1-I50.9	Heart failure
I5A	Non-ischemic myocardial injury (non-traumatic) (Code effective 10/1/2021)
J44.1	Chronic obstructive pulmonary disease with (acute) exacerbation
J45.901	Unspecified asthma with (acute) exacerbation
J90	Pleural effusion, not elsewhere classified
J91.8	Pleural effusion in other conditions classified elsewhere
J94.8	Other specified pleural conditions
J94.9	Pleural condition, unspecified
J96.00- J96.02	Acute respiratory failure
J96.20- J96.22	Acute and chronic respiratory failure
J96.90- J96.92	Respiratory failure, unspecified
R06.00	Dyspnea, unspecified
R06.01	Orthopnea
R06.02	Shortness of breath
R06.03	Acute respiratory distress
R06.09	Other forms of dyspnea
R06.2	Wheezing
R06.3	Periodic breathing
R06.4	Hyperventilation
R06.81	Apnea, not elsewhere classified
R06.82	Tachypnea, not elsewhere classified
R06.89	Other abnormalities of breathing
R06.9	Unspecified abnormalities of breathing

ICD-10-CM Diagnosis Codes	Description
R07.1- R07.9	Chest pain
R60.0- R60.9	Edema

Considered Experimental/Investigational/Unproven:

ICD-10-CM Diagnosis Codes	Description
	All other codes

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